



UNITED STATES PATENT AND TRADEMARK OFFICE

UNITED STATES DEPARTMENT OF COMMERCE
United States Patent and Trademark Office
Address: COMMISSIONER FOR PATENTS
P.O. Box 1450
Alexandria, Virginia 22313-1450
www.uspto.gov

| APPLICATION NO. | FILING DATE | FIRST NAMED INVENTOR | ATTORNEY DOCKET NO. | CONFIRMATION NO. |
|-----------------|-------------|----------------------|---------------------|------------------|
| 10/074,014 | 02/14/2002 | Tetsunori Matsushita | Q68466 | 6205 |

7590 10/22/2003

SUGHRUE MION, PLLC
2100 Pennsylvania Avenue, NW
Washington, DC 20037-3213

| |
|----------|
| EXAMINER |
|----------|

BALASUBRAMANIAN, VENKATARAMAN

| | |
|----------|--------------|
| ART UNIT | PAPER NUMBER |
|----------|--------------|

1624

DATE MAILED: 10/22/2003

9

Please find below and/or attached an Office communication concerning this application or proceeding.

Office Action Summary

Application No.

10/074,014

Applicant(s)

MATSUSHITA, TETSUNORI

Examiner

Venkataraman Balasubramanian

Art Unit

1624

-- The MAILING DATE of this communication appears on the cover sheet with the correspondence address --

Period for Reply

A SHORTENED STATUTORY PERIOD FOR REPLY IS SET TO EXPIRE 3 MONTH(S) FROM THE MAILING DATE OF THIS COMMUNICATION.

- Extensions of time may be available under the provisions of 37 CFR 1.136(a). In no event, however, may a reply be timely filed after SIX (6) MONTHS from the mailing date of this communication.
- If the period for reply specified above is less than thirty (30) days, a reply within the statutory minimum of thirty (30) days will be considered timely.
- If NO period for reply is specified above, the maximum statutory period will apply and will expire SIX (6) MONTHS from the mailing date of this communication.
- Failure to reply within the set or extended period for reply will, by statute, cause the application to become ABANDONED (35 U.S.C. § 133).
- Any reply received by the Office later than three months after the mailing date of this communication, even if timely filed, may reduce any earned patent term adjustment. See 37 CFR 1.704(b).

Status

- 1) ☒ Responsive to communication(s) filed on 04 August 2003.
- 2a) ☐ This action is **FINAL**. 2b) ☒ This action is non-final.
- 3) ☐ Since this application is in condition for allowance except for formal matters, prosecution as to the merits is closed in accordance with the practice under *Ex parte Quayle*, 1935 C.D. 11, 453 O.G. 213.

Disposition of Claims

- 4) ☒ Claim(s) 9-15 is/are pending in the application.
- 4a) Of the above claim(s) 9, 11 and 13-15 is/are withdrawn from consideration.
- 5) ☐ Claim(s) _____ is/are allowed.
- 6) ☒ Claim(s) 10 and 12 is/are rejected.
- 7) ☐ Claim(s) _____ is/are objected to.
- 8) ☐ Claim(s) _____ are subject to restriction and/or election requirement.

Application Papers

- 9) ☐ The specification is objected to by the Examiner.
- 10) ☐ The drawing(s) filed on _____ is/are: a) ☐ accepted or b) ☐ objected to by the Examiner.
- Applicant may not request that any objection to the drawing(s) be held in abeyance. See 37 CFR 1.85(a).
- 11) ☐ The proposed drawing correction filed on _____ is: a) ☐ approved b) ☐ disapproved by the Examiner.
- If approved, corrected drawings are required in reply to this Office action.
- 12) ☐ The oath or declaration is objected to by the Examiner.

Priority under 35 U.S.C. §§ 119 and 120

- 13) ☐ Acknowledgment is made of a claim for foreign priority under 35 U.S.C. § 119(a)-(d) or (f).
- a) ☐ All b) ☐ Some * c) ☐ None of:
1. ☐ Certified copies of the priority documents have been received.
2. ☐ Certified copies of the priority documents have been received in Application No. _____.
3. ☐ Copies of the certified copies of the priority documents have been received in this National Stage application from the International Bureau (PCT Rule 17.2(a)).
- * See the attached detailed Office action for a list of the certified copies not received.
- 14) ☐ Acknowledgment is made of a claim for domestic priority under 35 U.S.C. § 119(e) (to a provisional application).
- a) ☐ The translation of the foreign language provisional application has been received.
- 15) ☐ Acknowledgment is made of a claim for domestic priority under 35 U.S.C. §§ 120 and/or 121.

Attachment(s)

- 1) ☐ Notice of References Cited (PTO-892)
- 2) ☐ Notice of Draftsperson's Patent Drawing Review (PTO-948)
- 3) ☐ Information Disclosure Statement(s) (PTO-1449) Paper No(s) _____
- 4) ☐ Interview Summary (PTO-413) Paper No(s). _____
- 5) ☐ Notice of Informal Patent Application (PTO-152)
- 6) ☐ Other: _____

DETAILED ACTION

Applicants' response, which included amendment to claims 10 and 12, filed on 8/4/2003, is made of record.

Claims 9-15 are in the application. Of which claims 9, 11, 13-15 were withdrawn from consideration as noted in the previous office action. Claims 10 and 12 are under examination. In view of applicants' amendment to claims 10 and 12, all 112 second paragraph rejections made in the previous office action have been obviated.

However, the following apply.

Claim Rejections - 35 USC § 112

The following is a quotation of the second paragraph of 35 U.S.C. 112:

The specification shall conclude with one or more claims particularly pointing out and distinctly claiming the subject matter which the applicant regards as his invention.

Claims 10 and 12 are rejected under 35 U.S.C. 112, second paragraph, as being indefinite for failing to particularly point out and distinctly claim the subject matter which applicant regards as the invention.

Claims 10 and 12 are rejected under 35 U.S.C. 112, second paragraph, as being incomplete for omitting essential elements, such omission amounting to a gap between the elements. See MPEP § 2172.01. The omitted elements are: claims 10 and 12 which are independent claims, recite a process for making compound of formula 2 but does not recite how such a compound is made second intermediate. Note said claims merely recite, "preparing the isocyanatoformic ester derivative from the second intermediate" but do not recite how.

Claims 10 and 12 are rejected under 35 U.S.C. 112, first paragraph, because the specification, while being enabling for compound of formula 8 wherein O-R⁶ is a tetrahydrogeraniol group, does not reasonably provide enablement for genus of compounds bearing generically embraced in these claims when instant R⁶ is unsubstituted or substituted alkyl of at least 3 carbon atoms or unsubstituted or substituted aryl. The specification does not enable any person skilled in the art to which it pertains, or with which it is most nearly connected, to make and use the invention commensurate in scope with these claims.

Representative examples of structurally diverse compounds generically embraced in the invention when instant R⁶ is unsubstituted or substituted alkyl of at least 3 carbon atoms or unsubstituted or substituted aryl are not shown to form crystals after treatment with MOH. Instant process for compound formula 2 embrace compound of formula 8 with substituents bearing plethora of groups permitted at instant R⁶ variables which include variously substituted alkyl and aryl with variety of functional groups. There is no reasonable basis for assuming that the myriad of compounds embraced by the claims will all share the same profile as the exemplified compound bearing tetrahydrogeraniol since they are so structurally dissimilar as to be chemically non-equivalent and there is no basis in the prior art for assuming the same. Note In re Surrey 151 USPQ 724 regarding sufficiency of disclosure for Markush group. Also see MPEP 2164.03 for enablement requirements in cases directed to structure-sensitive art. Note Ex parte Gelles 22 USPQ 2nd 1318, especially the following quote: " The evidence relied upon also should be reasonably commensurate in scope with the subject matter

claimed and illustrate the claimed subject matter " as a class" relative to prior art subject matter."

Thus, factors such as "sufficient working examples", "the level of skill in the art" and "predictability", etc. have been demonstrated to be sufficiently lacking in the instant case for the instant method of use. In view of the breadth of the claims, the chemical nature of the invention, the unpredictability of enzyme-inhibitor interactions in general, and the lack of working examples regarding the activity of the claimed compounds towards treating the variety of diseases of the instant claims, one having ordinary skill in the art would have to undergo an undue amount of experimentation to use the instantly claimed invention commensurate in scope with the claims.

Claim Rejections - 35 USC § 103

The following is a quotation of 35 U.S.C. 103(a) which forms the basis for all obviousness rejections set forth in this Office action:

(a) A patent may not be obtained though the invention is not identically disclosed or described as set forth in section 102 of this title, if the differences between the subject matter sought to be patented and the prior art are such that the subject matter as a whole would have been obvious at the time the invention was made to a person having ordinary skill in the art to which said subject matter pertains. Patentability shall not be negated by the manner in which the invention was made.

The factual inquiries set forth in *Graham v. John Deere Co.*, 383 U.S. 1, 148 USPQ 459 (1966), that are applied for establishing a background for determining obviousness under 35 U.S.C. 103(a) are summarized as follows:

1. Determining the scope and contents of the prior art.
2. Ascertaining the differences between the prior art and the claims at issue.
3. Resolving the level of ordinary skill in the pertinent art.

4. Considering objective evidence present in the application indicating obviousness or nonobviousness.

Claims 10 and 12 are rejected under 35 U.S.C. 103(a) as being unpatentable over Takiguchi et al. JP 50 14631 in view of Fu et al. US 4,659,853 for reasons of record. To repeat:

Takiguchi et al. teaches a process for making S-alkyl isothiocyanatoformic esters, which involves alkylation of isothiocyanatoformic ester with dialkylsulfate or alkylhalide. See entire document, especially see pages 195-196 for the alkylation process and pages 198-202 for a Table showing compounds made. Particularly note NaOH is used for alkylation and therefore there is an inherent teaching of making the sodium salt of the isothiocyanatoformic ester for alkylation. For English version, see CAPLUS abstract provided.

Instant method differs in requiring a step in which isothiocyanatoformic ester is prepared by reacting chloroformic ester with metal thiocyanate and hydroxy compound.

The secondary reference Fu teaches a general process for making isothiocyanatoformic ester, which is same as embraced in the step one of claim 12. See entire document especially column 1 and column 2 for detail description of the process and examples 1-20 on column 3 through column 8.

Note the starting material and the product are analogous in that isothiocyanatoformic ester is formed in the secondary reference is used to make the product of the primary reference using an alkylating step. Thus one having ordinary skill in the art at the time of the invention was made would have been motivated to combine both the primary and secondary references and employ the process taught by these

Art Unit: 1624

prior art to the starting materials and reactants and expect to obtain the desired product because he would have expected the analogous reactions behave similarly. It has been held that application of an old process to an analogous material to obtain a result consistent with the teachings of the art would have been obvious to one having ordinary skill. Note *In re Kerkhoven* 205 USPQ 1069.

Applicants' traversal to overcome this rejection is not persuasive. The following apply to the traversal.

1. First of all, contrary to applicants' urging, the combined teachings of the primary and secondary reference clearly include the overall process of making isothiocyanatoformic ester. More specifically, the primary reference teaches the S- alkylation process which is not positively recited in the claims 10 and 12 as note above 112 rejection, while the secondary reference teaches the process of making the compound of formula 8 from which one can make the S-alkylated product. The instant claims isolates the product of formula 8 as salt and subsequently neutralizes to get compound of formula 8. But isolation of an intermediate or purification of an intermediate is not deemed as patentably distinct inventive process, as one trained in the art would know how to do so. In fact, applicants' own specification on page 41 recites that intermediate compound "can be purified by means of recrystallization or like". Hence, instant process is an obvious variant of prior art teachings. Applicants have asserted that isolation of the intermediate as a salt results in purity improvement but applicants have not provided proper comparative data.

Art Unit: 1624

Comparative example provided on pages 52-54 is deemed as not a proper comparison. First of all, it is not clear what prior art process being compared. If the purity of final product is the improvement that the instant invention is claiming as unexpected/ superior results, the proper prior art would be the primary reference cited above wherein hydroxide is used for the alkylation process not carbonate as done in the comparative example.

Secondly, as evident from the specification and claims, the gist of applicants' invention is isolation of the second intermediate for purity improvement, then the comparison should be with a prior art product of the secondary reference which adopts conventional purification with the instant product of formula 8 wherein salt formation and subsequent neutralization is used for purity improvement.

2. Secondly, applicants seem to assert that for when instant R^6 is unsubstituted or substituted alkyl of at least 3 carbon atoms or unsubstituted or substituted aryl then only the salt of formula 8 with MOH can obtained as crystals. See pages 15-16 of applicants' response. But applicants have not shown any examples to show that it is not possible to isolate the salt of compound of formula 8 when R^6 is ethyl or methyl. Specification has only one example with tetrahydrogeraniol and there is no support for the above assertion for all or any compound with 3 or more carbon atoms other than tetrahydrogeraniol. In fact, a careful reading of pages 24 through 30 appears to contradict applicants' assertion. Note species 2-4 and 2-6 are methyl and ethyl compounds and hence according to applicants assertion

they are not supposed to yield crystalline salt of product 8. Thus it is not clear how to reconcile with tow contradictory recitations.

3. Thirdly, applicants' assertion that Takiguchi et al., teaches "lower alkyl" but this is limited to methyl and ethyl only, is clearly a biased opinion. First of all, one trained in the art would regard lower alkyl as C₁-C₆ alkyl at the least more than two choices offered by applicants. The fact that Takiguchi et al. exemplified methyl and ethyl does not alter the definition of the term and that teaching of methyl and ethyl is adequate for one trained in the art to make the genus of "lower alkyl" embraced in the general definition of the term.

Applicants should also note that Takiguchi et al teaches species with benzyl group which would correspond to substituted alkyl and is same as instant 2-31.

Furthermore, Takiguchi et al teaches besides lower alkyl, alkenyl group and exemplifies allyl bearing species, which would definitely meet instant 3 carbon requirement.

Thus based on above reasons, the rejection is proper and is maintained.

This action is not made FINAL.

Conclusion

Any inquiry concerning this communication from the examiner should be addressed to Venkataraman Balasubramanian (Bala) whose telephone number is (703) 305-1674. The examiner can normally be reached on Monday through Thursday from 8.00 AM to 6.00 PM. The Supervisory Patent Examiner (SPE) of the art unit 1624 is Mukund Shah whose telephone number is (703) 308-4716.

Application/Control Number: 10/074,014
Art Unit: 1624

Page 9

The fax phone number for the organization where this application or proceeding is assigned (703) 308-4556.

Any inquiry of a general nature or relating to the status of this application or proceeding should be directed to the receptionist whose telephone number is (703) 308-1235.

V. Balasubramanian
Venkataraman Balasubramanian

10/15/2003